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Award Number: W81XWH-06-1-0245

TITLE: Contribution of AMACR and Phytanic Acid to Prostate Cancer Risk Among African Americans in North Carolina

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REPORT DATE: February 2008

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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| REPORT DOCUMENTATION PAGE | | | | Form Approved OMB No. 0704-0188 | |
|--|-------------|--------------------------|----------------------------|---|---|
| Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS. | | | | | |
| 1. REPORT DATE 14-02-2008 | | 2. REPORT TYPE Annual | | 3. DATES COVERED 15 JAN 2007 - 14 JAN 2008 | |
| 4. TITLE AND SUBTITLE Contribution of AMACR and Phytanic Acid to Prostate Cancer Risk Among African Americans in North Carolina | | | | 5a. CONTRACT NUMBER | |
| | | | | 5b. GRANT NUMBER W81XWH-06-1-0245 | |
| | | | | 5c. PROGRAM ELEMENT NUMBER | |
| 6. AUTHOR(S) Bao-Li Chang, Ph.D. Email: bchang@wfubmc.edu | | | | 5d. PROJECT NUMBER | |
| | | | | 5e. TASK NUMBER | |
| | | | | 5f. WORK UNIT NUMBER | |
| 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Wake Forest University Health Sciences Winston-Salem, NC 27157 | | | | 8. PERFORMING ORGANIZATION REPORT NUMBER | |
| 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012 | | | | 10. SPONSOR/MONITOR'S ACRONYM(S) | |
| | | | | 11. SPONSOR/MONITOR'S REPORT NUMBER(S) | |
| 12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited | | | | | |
| 13. SUPPLEMENTARY NOTES | | | | | |
| 14. ABSTRACT Several lines of evidence have suggested genetic and dietary differences may be important in PCa, particularly among AA (African American) men. In this study, we aim to test the hypothesis that mutations/sequence variants in the AMACR gene, and dietary intake of foods rich in phytanic acid, increase the risk to PCa among AA men. We will conduct a population based study by ascertaining 250 AA men who have PCa and 250 race, age, and county-matched controls from eight counties of North Carolina. We are in the process of carrying out the 1st task, study subject recruitment, through the year 2008. In the past funding year, we have expanded our study area and significantly increased our rate of subject recruitment. Additionally, we have also obtained additional grant funding related to the science of this project, which will help provide independent confirmation of the findings from this study in a different study population. The results from this study, as well as other future studies based on this study population, will greatly increase our knowledge for potential risk factors and suggest potential preventive strategies for prostate cancer in AA men. | | | | | |
| 15. SUBJECT TERMS Prostate Cancer, Phytanic Acid, AMACR, African American, Susceptibility, Association | | | | | |
| 16. SECURITY CLASSIFICATION OF: | | | 17. LIMITATION OF ABSTRACT | 18. NUMBER OF PAGES | 19a. NAME OF RESPONSIBLE PERSON |
| a. REPORT | b. ABSTRACT | c. THIS PAGE | | | USAMRMC |
| U | U | U | UU | 7 | 19b. TELEPHONE NUMBER (include area code) |

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Introduction

Several lines of evidence have suggested genetic and dietary differences may be important in PCa, particularly among AA men. Specifically, the *AMACR* gene has been implicated by gene expression profiling of tumors, as well as in genetic studies among mostly Caucasian American subjects. Additionally, the *AMACR* gene happens to be required for the metabolism of phytanic acid, which is obtained in the human diet almost exclusively in red meat and dairy products, both of which have been implicated in PCa risk. In this study, our primary goal is to test the hypothesis that mutations/sequence variants in the *AMACR* gene increase the risk to PCa among AA men. Our secondary goal is to test the hypothesis that PCa risk is increased by dietary intake of foods rich in phytanic acid, and that this risk is further increased due to alterations in *AMACR*. To test these hypotheses, we will conduct a population based study by ascertaining an additional 250 AA men who have PCa and 250 race, age, and county-matched controls from eight counties of North Carolina. These can be combined with our existing pilot study population, for a total of ~550 AA men. Our primary aim is to identify the AA spectrum of mutations and sequence variants in *AMACR* and assess their contribution to PCa. Our secondary aim is to preliminarily assess the contribution to PCa risk related to dietary intake of foods rich in phytanic acid, and then explore the interaction effect between *AMACR* and phytanic acid.

Body

Summary from previous annual report

The first 25 months (15 Jan 2006 - 14 Feb 2008) of this study will be mainly focused on study subject recruitment. We spent the first 8 months (Jan-Aug 2006) of the funding period working to obtain regulatory approval from the IRB of the USAMRMC (DOD). We then spent two months (Sept-Oct 2006) obtaining approval from the North Carolina Cancer Registry Committee and our local IRB at Wake Forest University School of Medicine, thus allowing us to begin recruitment. The cancer registry began identification of cases for our study in early November 2006, and then reported the first

batch of cases to us in late November. We began to recruit these subjects in early December 2006. At the time of our previous report on the period ending February 14, 2007, we had recruited 20 cases via The North Carolina Central Cancer Registry, per inclusion and exclusion criteria.

Summary for current annual report

Because of the late start in subject recruitment due to IRB delays, we worked with the NC Central Cancer Registry to expand our study area. In addition to our previous 7 counties, we were able to expand into eight additional North Carolina counties, effective October 2007. Since this expansion, we have more than doubled the number of interviews we conduct each week, now averaging 8 to 9 per week. At this rate, we expect to complete recruitment by the end of this year. Although this recruitment will be completed later than our originally planned schedule, our recruitment timeframe was simply pushed back by delays in obtaining IRB approval. Since the previous report, we have recruited 88 additional subjects, for a new total of 108 subjects.

The specific accomplishments associated with each task in the Statement of work are detailed in the following section.

Statement of Work

Task 1. To recruit 250 AA men who have PCa and 250 race, age, and county-matched controls from eight counties of North Carolina, in a population based study. These can be combined with our pilot study population, for a total of ~550 AA men. (Originally proposed for Months 1-25; 15 Jan 2006 - 14 Feb 2008)

1. We were able to expand our study area into eight additional North Carolina counties, for a total of 15 counties.
2. We have doubled our recruitment rate. The current recruitment rate is 8 to 9 per week, which translates to completing our recruitment prior to the end of 2008.
3. We recruited 88 additional subjects, for a new total of 108 subjects, via The North Carolina Central Cancer Registry (NCCCR), per inclusion and

exclusion criteria.

Tasks 2, 3, and 4, will start after all study subjects have been recruited (task 1) during the 3rd year of this study.

Task 2. To identify sequence variant/mutation spectrum of the AMACR gene in AA men (Originally proposed for 15 Feb 2008 - 14 Apr 2008).

1. We can begin work on Aim 2 prior to the end of recruitment.
2. Current projection for Aim 2 is around October – November 2008

Task 3. To genotype mutations/sequence variants in AMACR among AA men and evaluate their contribution to and association with PCa (Originally proposed for 15 Apr 2008 - 14 July 2008 Months 26-28)

1. Current projection for Aim 3 is around December 2008 – February 2009

Task 4. To measure serum levels of phytanic acid and intake of dairy products and meat consumption for each subject, and test whether the these levels increase the risk to PCa among AA men (Originally proposed for 15 July 2008 - 14 Jan 2009)

1. We can begin work on Aim 4 prior to the end of recruitment.
2. Current projection for Aim 4 is around October 2008 – February 2009

Key Research Accomplishments

- Expanded study area
- Increased subject recruitment

Reportable Outcomes

We have obtained intramural funding from our institution for a similar study, but in an additional study population. The other study population was originally recruited by our collaborator in Sweden. If successful, the results from the current study and the Swedish study will provide independent confirmation of our hypothesis.

Conclusion

During the past funding period (15 Jan 2007 – 14 Feb 2008), we have expanded our study subject recruitment. Due to a faster rate of recruitment, we may still be able to make up for a later start in subject recruitment due to IRB approval delays. We will also try to begin lab analyses for Aims 2 and 4 prior to the completion of recruitment. We are committed to completing the recruitment of the study population and the analytical work. We are also actively looking for opportunities for additional studies based on this study population.

The direct results from this study, as well as other future studies based on this study population, will greatly increase our knowledge of potential risk factors and suggest for potential preventive strategies for prostate cancer in AA men. These men have the highest risk to develop prostate cancer, and the highest risk to eventually develop aggressive forms of prostate cancer, while also being an understudied group. Therefore, this project fills a vital gap in our understanding of prostate cancer etiology. This study could potentially clarify the diet-gene interactions that lead to prostate cancer. Specifically, this project could lead to genetic testing that would help identify men with increased prostate cancer risk, while at the same time offering these men targeted guidance to reduce this risk by lowering their dietary intake of certain foods such as dairy, red meat, and fatty fish.

References.

None.

Appendices.

None.